III. REMARKS

Claims 102-114 are pending. Claims 84-101 have been cancelled without prejudice. Claims 102 and 103 have been amended without prejudice. Claims 104-114 have been added. Claims 104-109 and 111-112 correspond with previously presented dependent claims 85-90 and 91-92 and are now dependent on claim 102. Support for new claims 110 and 113-114 can be found, e.g., at page 5, lines 15-24 and page 12, line 20 to page 13 line 2 of the specification.

A. Claim objections

Claims 84-93 and 102 were objected as to the expression "APP" in the claims "since the expression "APP" is used to identify/describe particular process herein and, accordingly, the identification/description is unclear." The Examiner noted that "claims 184-93 (sic) and 103 will be examined using the 'amyloid precursor protein" as defined on page 1 of the specification as has apparently been intended."

The current pending claims no longer recite the term APP. Therefore, the Examiner is requested to remove this objection.

B. Rejection of claims 84-103 under 35 U.S.C. §112, second paragraph

Claims 84-103 were rejected under 35 U.S.C. 112, second paragraph, for indefiniteness. Specifically, the Examiner states that "[t]he terms 'suitable' in claim 84, 94, and 102-103 and 'positive' in claim 98 are relative terms which renders claims 84-103 indefinite." In addition, the Examiner states that "[t]he recitations, 'an osmotic agent' and 'a optional first coating and a second coating,' in claims 91 and 101 render claim 91-93 and 101 indefinite."

This rejection is traversed. With respect to the terms "suitable", and the term "positive", the pending claims have been amended without prejudice, to no longer contain these terms. Therefore, the Examiner's rejection with respect to these terms is moot.

With respect to the term "an osmotic agent", the Examiner's attention is respectfully directed to page 13, lines 12-18, which describes osmotic agents. It is respectfully submitted that in view of the specification, in particular page 13, lines 12-18, one of ordinary skill in the art would understand what is meant by osmotic agents.

With respect to the term "an optional first coating and a second coating," the term "optional; has been deleted without prejudice from this phrase. With respect to "a first coating and a second coating" the Examiner's attention is respectfully directed to page 15, lines 4 to 15 which describes such coatings. It is respectfully submitted that in view of the specification, in particular page 15, lines 4 to 15, one of ordinary skill in the art would understand what is meant by such coatings.

In view of the aforementioned, it is respectfully submitted that the claims are not indefinite and the rejection should be removed.

C. Rejection of claims 84-90, 92-93 and 103 under 35 U.S.C. § 102

Claims 84-90, 92-93 and 103 were rejected under 35 U.S.C. 102(b) "as being anticipated by Scolnick (WO 95/06470)." The Examiner states that "Scolnick discloses methods of treating Alzheimer's disease or the onset of Alzheimer's disease in a human patient comprising administering to the said patient a therapeutically effective amount of a composition comprising an HMG-CoA reductase inhibitor, in particular, lovastatin (20 mg per day), simvastatin, pravastatin, and fluvastatin." (citations omitted). The Examiner further states that "Scolnick also discloses that the HMG-CoA reductase inhibitor is administered orally by a timed-controlled release dosage form including osmotic devices, diffusion controlled systems, dissolution controlled matrices and erodible/degradable matrics," (citations omitted) and notes that "the therapeutically effective amount of the HMG-CoA reductase inhibitor to be administered per day in the instant invention has been disclosed in Scolnick." The Examiner also states that "Scolnick further discloses that the treatment therein with the lovastatin composition underwent four consecutive nine-week periods, within the instant claimed period." (citations omitted). The Examiner concludes that "Scolnick's method inherently treats or reduces beta amyloid levels in a

human which exhibits symptoms of Alzheimer's disease, and Down's syndrome (both known as amyloid precursor protein processing disorders), as claimed herein since Scolnick's method steps are same as the instant method steps." (citations omitted). "Moreover, Scolnick's method inherently decreases in mean beta amyloid concentration in the blood of said human patient by at least about 18 pg/ml after 1 month of treatment since decreasing in mean beta amyloid concentration in the blood of said human patient by at least about 18 pg/ml after 1 month of treatment is considered to be an inherent property of the administration of a HMG-CoA reductase inhibitor composition for the treatment herein", and "it is well settled that recitation of an inherent property of a composition will not further limit claims drawn to a composition." The Examiner states that "Scolnick clearly anticipates claim 84-90, 92-93, and 103."

This rejection is traversed. Initially, it is noted that claims 42-90, 92-93 were cancelled by this amendment and claim 102 was not rejected under 35 U.S.C. §102 by the Examiner. In any event, claim 103 which was subject to the 35 U.S.C. §102 rejection is still pending in the application.

With respect to claim 103, Scolnick, et al. fail to teach a method for treating Down's Syndrome in humans as recited in claim 103.

With respect to rejections under the doctrine of inherency, it is noted that as set forth in the MPEP, 8th edition, section 2122, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); In re Oelrich, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be recognized by one of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from

a given set of circumstances is not sufficient." In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).

It is further set forth in the MPEP, 8th edition, section 2122 that "[i]n relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the alleged inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. And Inter. 1990) (emphasis in original).

Further, the Federal Circuit stated the following in Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264, 1268-69, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991):

> *Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.*

Present claim 103 (and claim 102) calls for, inter alia, orally administering a controlled release formulation comprising at least one HMG-CoA reductase inhibitor which after oral administration to a human patient releases said at least one HMG-CoA reductase inhibitor at a rate to maintain therapeutically effective levels over a 24 hour dosing interval, and continuing treatment with said controlled release formulation to effect a decrease in mean beta amyloid concentration in the blood of said human patient by at least about 18 pg/ml after 1 month of treatment.

Scolnick et al. fail to teach "orally administering a controlled release formulation comprising at least one HMG-CoA reductase inhibitor which after oral administration to a human patient releases said at least one HMG-CoA reductase inhibitor at a rate to maintain therapeutically effective levels over a 24 hour dosing interval" as recited in the present claims. Further, Scolnick et al. fail to teach "continuing treatment with said controlled release

formulation to effect a decrease in mean beta amyloid concentration in the blood of said human patient by at least about 18 pg/ml after 1 month of treatment" as recited in the present claims.

It is respectfully submitted that such limitations are not inherent in Scolnick as these limitations do not "necessarily flow" from the description of Scolnick. Scolnick does not exemplify administration of a *controlled release formulation*, and although Scolnick does mention the possibility of oral administration of the medicament "in the form of a time-controlled release vehicle" at page 11, lines 8-15, Scolnick fails to teach maintaining therapeutically effective levels over a 24 hour dosing interval. Maintaining therapeutically effective levels over a 24 hour dosing interval does not necessarily flow from Scolnick, as controlled release dosage forms do not necessarily provide therapeutically effective levels over a 24 hour period (e.g., some controlled release dosage forms provide therapeutically effective levels over a 12 hour dosing interval). Further, it is respectfully submitted that the Examiner has not provided a basis in fact and/or technical reasoning to reasonably support the determination that "maintaining therapeutically effective levels over a 24 hours dosing interval" necessarily flows from the Scolnick et al.

Scolnick et al. also do not teach continuing treatment with said controlled release formulation to effect a decrease in mean beta amyloid concentration in the blood of said human patient by at least about 18 pg/ml after 1 month of treatment. Further, it is respectfully submitted that the Examiner has not provided a basis in fact and/or technical reasoning to reasonably support the determination that "a decrease in mean beta amyloid concentration in the blood of said human patient by at least about 18 pg/ml after 1 month of treatment" necessarily flows from the Scolnick et al.

It is respectfully submitted that the Examiner has provide no basis to make the assumption that Scolnick's exemplified administration of 20 mg immediate release lovastatin or 40 mg immediate release simvastatin per day inherently have the same effect as controlled release formulations as presently described and claimed.

In view of the reasons set forth above and others, it is respectfully submitted that Scolnick does not anticipate the claims and the rejection should be removed.

D. Rejection of claims 91, 94-102 under 35 U.S.C. § 103

Claims 91 and 94-102 were rejected under 35 U.S.C. 103(a) "as being unpatentable over Scolnick (WO 95/06470) in view of Chen et al. (5,916,595, PTO-892) and McKhann et al. (PTO-892). The Examiner relies on the same discussion of Scolnick with respect to the 35 U.S.C. 102 rejection above, and the Examiner states that "[i]t would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the controlled release formulation of HMG-CoA reductase inhibitor disclosed in Chen et al., comprising an alkyl ester of a substituted naphthalene, an osmotic agent and coating agents with a pH sensitive water insoluble polymer, and to employ the method for determining whether a human exhibits at least one symptom of Alzherimer's disease taught in McKhann et al. in the instant claimed methods.

The Examiner further states that "[o]ne having ordinary skill in the art at the time the invention was made would have been motivated to employ the controlled release formulation of HMG-CoA reductase inhibitor, disclosed in Chen et al., comprising an alkyl ester of a substituted naphthalene, and an osmotic agent and coating agents with a pH sensitive water insoluble polymer, in the instant claimed methods, because the controlled release formulation of Chen et al. is known to be a better controlled release system and have advantages, e.g.., substantially and completely delivering a HMG-CoA reductase inhibitor, lovastatin in particular without the need to provide a passageway, and additionally providing higher bioavailability." "Moreover, one having ordinary skill in the art at the time the invention was made would have been motivated to employ a method step for determining whether a human exhibits at least one symptom of Alzheimer's disease in the instant claimed methods since a method for determining whether a human exhibits at least one symptom of Alzheimer's disease is well known in the art, i.e., taught in McKhann et al. Thus, it is well within the skill of artisan to deterring whether a human exhibits at least one symptom of Alzheimer's disease using the known method and then treat the patient."

This rejection is traversed. Scolnick et al. fail in the very least to teach, hint, or suggest "determining whether a human exhibits an elevated level of β-amyloid" as recited in current claim 102. In addition, Scolnick et al. fail to teach, hint or suggest "orally administering a controlled release formulation comprising at least one HMG-CoA reductase inhibitor which after oral administration to a human patient releases said at least one HMG-CoA reductase inhibitor at a rate to maintain therapeutically effective levels over a 24 hour dosing interval" and "continuing treatment with said controlled release formulation to effect a decrease in mean beta amyloid concentration in the blood of said human patient by at least about 18 pg/ml after 1 month of treatment" as recited in the present claims.

Chen et al. (5,916,595, PTO-892) discloses a controlled release dosage formulation which is based on a combination of: (a) a compressed tablet core which contains an alkyl ester of hydroxyl substituted naphthalene derivative, a pharmaceutically acceptable, water swellable polymer and an osmotic agent; and (b) an outer coating layer which completely covers the osmotic core and comprises a pH sensitive coating agent and a water insoluble polymer. See Abstract. Chen fails in the very least to teach, hint or suggest, determining whether a human exhibits an elevated level of β-amyloid as recited in claim 102.

McKhann et al. is directed to "Clinical diagnosis of Alzheimer's disease." McKhann et al. fails in the very least to teach, hint, or suggest determining whether a human exhibits an elevated level of β-amyloid as recited in claim 102. In addition, there is no teaching, hint or suggestion in McKhann et al. of β-amyloid.

Further the combination of Scolnick et al., Chen et al. (5,916,595, PTO-892), and McKhann et al. fail in the very least to teach, hint, or suggest determining whether a human exhibits an elevated level of β-amyloid as recited in claim 102. It is respectfully submitted that one would not be motivated to determine an elevated level of β-amyloid as there is no teaching in either of these references alone or in combination that such elevated level is useful as an indicator of Alzeheimer's disease.

Therefore, the Examiner is requested to remove this rejection as Chen et al. (5,916,595, PTO-892), and McKhann et al. do not cure the deficiencies of Scolnick et al.

E. Conclusion

It is now believed that the above-referenced rejection has been obviated and withdrawal is respectfully requested. It is believed that all claims are now in condition for allowance.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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